Early plasma transfusion is associated with improved survival after isolated traumatic brain injury in patients with multifocal intracranial hemorrhage

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Background. *Plasma-based resuscitation improves outcomes in trauma patients with hemorrhagic shock, while large-animal and limited clinical data suggest that it also improves outcomes and is neuroprotective in the setting of combined hemorrhage and traumatic brain injury. However, the choice of initial resuscitation fluid, including the role of plasma, is unclear for patients after isolated traumatic brain injury.*
Methods. *We reviewed adult trauma patients admitted from January 2011 to July 2015 with isolated traumatic brain injury. "Early plasma" was defined as transfusion of plasma within 4 hours. Purposeful multiple logistic regression modeling was performed to analyze the relationship of early plasma and inhospital survival. After testing for interaction, subgroup analysis was performed based on the pattern of brain injury on initial head computed tomography: epidural hematoma, intraparenchymal contusion, subarachnoid hemorrhage, subdural hematoma, or multifocal intracranial hemorrhage.*
Results. *Of the 633 isolated traumatic brain injury patients included, 178 (28%) who received early plasma were injured more severely coagulopathic, hypoperfused, and hypotensive on admission. Survival was similar in the early plasma versus no early plasma groups (78% vs 84%, P = .08). After adjustment for covariates, early plasma was not associated with improved survival (odds ratio 1.18, 95% confidence interval 0.71–1.96). On subgroup analysis, multifocal intracranial hemorrhage was the largest subgroup with 242 patients. Of these, 61 (25%) received plasma within 4 hours. Within-group logistic regression analysis with adjustment for covariates found that early plasma was associated with improved survival (odds ratio 3.34, 95% confidence interval 1.20–9.35).*
Conclusion. *Although early plasma transfusion was not associated with improved in-hospital survival for all isolated traumatic brain injury patients, early plasma was associated with increased in-hospital survival in those with multifocal intracranial hemorrhage. (Surgery 2016;■:■-■.)*

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Traumatic brain injury (TBI) is estimated to cause up to half of trauma deaths[1] and is a significant cause of morbidity and long-term disability. Presently, there is no effective therapy for primary brain injury caused by the traumatic insult. Current treatments are, therefore, aimed at reducing the risk factors of secondary brain injury: hypoxia, hypoperfusion, hypoglycemia, and excitotoxicity.[2]

Hypotension, in particular, is extremely harmful; a study by Chesnut et al[3] found that a single episode of hypotension (systolic blood pressure [SBP] <90 mmHg) was associated with a 150% increase in mortality after severe TBI. Fluid resuscitation is instrumental in mitigating these risk factors after TBI, but the optimal regimen, including type,

timing, and volume of fluids, is unknown.[4] Isotonic crystalloid, such as normal saline, has been the fluid of choice traditionally, but its use is not supported by good evidence.

The advent of "damage control resuscitation" with the use of plasma as the primary volume expander is associated with improved outcomes in trauma patients presenting with hemorrhagic shock.[5-7] This effect may be due to the ability of plasma to repair endothelial injury and reduce vascular permeability, which has been demonstrated in vitro and in animal models of hemorrhagic shock.[8-10]

In a large-animal model of combined TBI and hemorrhagic shock, plasma-based resuscitation reduced secondary brain injury[11] and improved neurologic recovery.[12] This benefit was attributed to improved cerebral perfusion, mitigation of glutamine-mediated excitotoxicity, and reduced mitochondrial dysfunction with plasma resuscitation.[13] Data on the role of plasma in the treatment of isolated TBI, however, are scarce. We hypothesized that early plasma transfusion would be associated with improved in-hospital survival in patients who presented with isolated TBI.

METHODS

Study design. Approval was obtained from the University of Texas Health Science Center at Houston Institutional Review Board. We queried our trauma registry to perform a single-institution, retrospective study of consecutive, highest-level adult trauma patients (≥16 years of age) admitted between January 2011 and July 2015. To identify patients with isolated TBI, we first screened for patients with head/neck Abbreviated Injury Scale (AIS) ≥3 and AIS of all other body regions <3. Patients were then excluded if they had a negative initial head computed tomography (CT) scan, <2 head CT scans, known prehospital warfarin use, or uncontrolled hemorrhage, which was defined as activation of a massive transfusion protocol or continued hemorrhage despite basic hemostatic maneuvers, such as external compression or wound packing.

Patient demographics, including age, sex, Glasgow Coma Score (GCS), admission vital signs, admission base excess, admission activated clotting time on thromboelastography, injury severity score, AIS score, intensive care unit (ICU)–free days, in-hospital survival, discharge location, and mechanism of injury (blunt versus penetrating) were obtained from patient records. Patients were dichotomized into "early plasma" and "no early plasma" groups based on transfusion of any plasma within 4 hours of hospital presentation. In-hospital survival was defined as being alive at time of discharge and discharge to anywhere other than hospice.

Head CT analysis. Initial head CTs are obtained based on admission GCS, mechanism of injury, and the discretion of the attending trauma surgeon. After the head CTs are interpreted by the trauma team and a radiologist, appropriate consultations are requested from neurosurgery. If the initial head CT is abnormal, a second head CT is obtained within 6 hours to evaluate for stability versus progression of the presenting brain injury. However, a second head CT is not obtained if the injury is deemed "nonsurvivable" by the attending neurosurgeon. Therefore, the criterion of ≥2 head CT scans identifies patients with severe, but potentially survivable, injury who may benefit from early plasma transfusion.

Patients were categorized into mutually exclusive subgroups based on the dominant brain lesion on the initial head CT: epidural hematoma (EDH), subdural hematoma (SDH), intraparenchymal contusion (IPC), subarachnoid hemorrhage (SAH), or multifocal intracranial hemorrhage (MIH). MIH was defined as ≥2 different types of brain lesion without a dominant lesion (Fig 1). Progression of head injury (PHI) was defined as an increase in the size of intracranial hemorrhage compared to findings on the initial head CT as determined by the attending radiologist.

Laboratory analysis. Blood samples are obtained from highest-level trauma patients immediately upon arrival to the emergency department (ED) and are sent for blood gas analysis, basic metabolic panel, complete blood count, and rapid thromboelastography (r-TEG). r-TEGs are run on a Thromboelastograph 5000 (Hemoscope Corp, Niles, IL) with clinically relevant data available within 5 minutes. The activated clotting time (ACT) is a measure of the amount of time needed to initiate clot formation and is dependent on plasma clotting factor activity. At our institution, we use ACT ≥128 seconds as a plasma transfusion trigger when bleeding is suspected or confirmed; a previous study performed at our institution found that this cutoff predicted need for massive transfusion within 6 hours of presentation in multiply injured trauma patients.[14]

Statistical analysis. Statistical analysis was performed using Stata software (Stata 14.1; StataCorp LP, College Station, TX). Data are reported as median values with interquartile range or proportions as appropriate. Nonparametric comparisons